

Brunton E, Blau C, Silveira C, Nazarpour K. [Identification of Sensory Information in Mixed Nerves using Multi-channel Cuff Electrodes for Closed Loop Neural Prostheses](#). In: *8th International IEEE EMBS Neural Engineering Conference*. 2017, Shanghai, China: IEEE.

**Copyright:**

© 2017 IEEE. Personal use of this material is permitted. Permission from IEEE must be obtained for all other uses, in any current or future media, including reprinting/republishing this material for advertising or promotional purposes, creating new collective works, for resale or redistribution to servers or lists, or reuse of any copyrighted component of this work in other works.

**DOI link to article:**

<https://doi.org/10.1109/NER.2017.8008372>

**Date deposited:**

27/09/2017

# Identification of Sensory Information in Mixed Nerves using Multi-channel Cuff Electrodes for Closed Loop Neural Prostheses

Emma Brunton, Christoph Blau, Carolina Silveira, and Kianoush Nazarpour, *Senior Member, IEEE*

**Abstract**—The addition of sensory feedback is expected to greatly enhance the performance of motor neuroprostheses. In the case of stroke or spinal cord injured patients, sensory information can be obtained from electroneurographic (ENG) signals recorded from intact nerves in the non-functioning limb. Here, we aimed to identify sensory information recorded from mixed nerves using a multi-channel cuff electrode. ENG afferent signals were recorded in response to mechanical stimulation of the foot corresponding to three different functional types of sensory stimuli, namely: nociception, proprioception and touch. Offline digital signal processing was used to extract features for use as inputs for classification. A quadratic support vector machine was used to classify the data and the five fold cross validation error was measured. The results show that classification of nociceptive and proprioceptive stimuli is feasible, with cross validation errors of less than 10%. However, further work is needed to determine whether the touch information can be extracted more reliably from these recordings.

## I. INTRODUCTION

Stroke or spinal cord injury can result in severe sensorimotor deficits that lower the patient's quality of life [1], [2]. Implanted functional electrical stimulation (FES) systems are capable of restoring some motor movement by stimulating the non-functioning limb and contracting muscles in a functional pattern [2], [3]. Currently implanted systems, however, operate in one direction stimulating the muscles to move without any closed loop feedback that would ensure that the stimulation had the desired functional effect. It is believed that closed-loop systems that provide sensory feedback will significantly improve the function and usefulness of motor prostheses [1]. As the patients using FES systems still have intact sensory receptors, the information travelling through their own nerves can be used to provide feedback signals [2], [3]. These signals can be recorded using a number of different neural interfaces for example, nerve cuffs [3], Utah arrays [4] and transversal interfascicular electrodes (TIME) [5].

Several studies have already attempted to shed light on the number and type of sensory events that can be discriminated in peripheral nerve recordings using different neural interfaces. The neural interfaces that have been examined include

but are not limited to tripolar cuffs [3], TIME [5] and LIFE [6]. Nerve cuffs are appealing as they are placed around the nerve so the underlying neural structure is not damaged and they have been shown to provide a long-term stable recording [3]. These advantages of the nerve cuff however, come with the disadvantages of a lower signal to noise ratio and less selectivity than intrafascicular electrode arrays [3], [5]. In [3], using a tripolar cuff, only sensory events carried by different fiber types could be discriminated, whereas TIMES [5] and LIFEs [6] have been shown to be capable of discriminating a number of different stimuli that would be carried by the same fiber type. To increase the selectivity of nerve cuffs, the number of contacts contained within cuff electrode arrays has been increased [7]. The number of sensory events that can be discriminated by multi-channel cuffs however, has previously not been examined. Of interest is whether these cuffs can differentiate signals carried by the same fiber types.

Zariffa et al. [7] examined the use of cuffs with a large number of contacts to discriminate signals travelling along different nerve branches. They showed that using a large number of recording contacts on a cuff improves the performance of a classifier, trained to discriminate signals when compared to a smaller number of contacts arranged in a ring [7]. However, in Zariffa et al. study only electrical stimulation was used to determine the selectivity of the cuff [7]. Here, we were interested in developing a greater understanding of the number and type of sensory events that could be separated from within whole nerve recordings in response to mechanical manipulation of the foot.

Previously, we reported on preliminary results where we were able to separate plantar and dorsi-flexion in neural recordings made with a multi-channel cuff [8]. These two types of stimuli could be decoded after extracting the mean absolute value of the signal from as little as two electrodes located circumferentially around a cuff. Our objective in this study was therefore to investigate if a larger number of sensory events could be identified in nerve recordings from multi-channel cuffs.

## II. METHOD

### A. Nerve Cuff

The multi-channel concentric nerve cuff was manufactured by Microprobes for Life Science (Gaithersburg, MD, USA). It consisted of 16 electrode contacts (4 rings of 4 Pt electrodes) mounted on silicon rubber tubing (Fig. 1). The inner diameter of the cuff was 1 mm, this is similar to the diameter of the sciatic nerve in the rats that were used in this study. The rings were spaced 0.75 mm apart and the distance from

This work is supported by EPSRC, UK (grants: EP/M025977/1 and EP/M025594/1).

Emma Brunton and Carolina Silveira are with the School of Electrical and Electronic Engineering, Newcastle University, Newcastle NE1 7RU, UK. (email: emma.brunton@newcastle.ac.uk)

C. Blau is with the Faculty of Medical Sciences, Newcastle University, Newcastle NE1 7RU, UK.

K. Nazarpour is with the School of Electrical and Electronic Engineering and the Institute of Neuroscience, Newcastle University, Newcastle NE1 7RU, UK. (email: kianoush.nazarpour@newcastle.ac.uk)

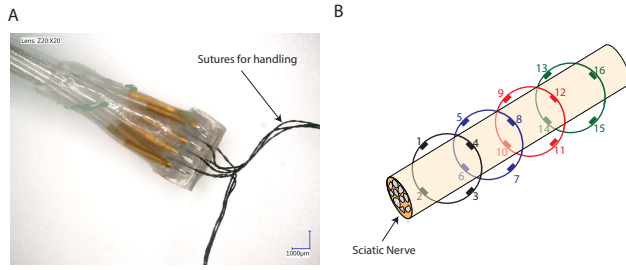


Fig. 1. A) Microscope image of the 16 channel nerve cuff used B) Relative positions of the electrodes in the rings within the cuff, electrodes 1, 5, 9 and 13 are on the same side of the cuff along its length and electrodes 1, 2, 3 and 4 are contained within the same ring.

the end of the contacts to the end of the cuff was 1 mm. All 16 electrode contacts were used for recording and referenced to a stainless steel wire placed in the skin.

### B. Animal Preparation

Three Sprague Dawley rats weighing between 400 and 500 g were used for this study. Following the procedure introduced in [9], induction of anesthesia was performed via an intraperitoneal injection of a combination of midazolam and hypnorm at 2.7 ml/kg. Anesthesia was maintained with intraperitoneal injections of the midazolam/hypnorm cocktail as well as isoflurane in oxygen delivered through a nose cone. Importantly, during neural recordings the Isoflurane was maintained at a level below 0.5% as Isoflurane has been shown to influence neural recordings [10]. Fluids were delivered intravenously through a tail vein cannula at 0.2 mL/hour (0.18% NaCl with 10% glucose diluted 1 in 2).

Under anaesthetic a 3 cm incision was made approximately 0.8 mm caudal to the femur, beginning at the level of the spine and ending at the knee. The two planes of the biceps femoris were gently dissected to expose the sciatic nerve. The nerve was then carefully freed from the surrounding tissue. The lead of the cuff was tunnelled under the muscle and skin to reduce the propensity for nerve compression or stretch. The nerve cuff was then carefully placed around the nerve and secured with Kwik-Cast (World Precision Instruments, FL, USA). The muscle and skin were sutured closed over the cuff to prevent the tissue from drying out, and to allow for movement of the animal into a sling for preparation. A tungsten wire was placed around the L5 spinous process and secured in place with dental acrylic for the ground. A stranded stainless steel wire was used as a reference, and was placed in the skin close to the incision site for the nerve cuff implantation. The reference was then secured with tissue glue.

### C. Neural Recordings and stimulus application

At the end of the surgery the rat was moved into a sling (Lomir Biomedical inc., Canada) so that the right hindpaw was free to be manipulated (Fig. 2A). All other limbs remained contained within the sling. The ENG signals were recorded at 30k samples per second using a Cerebus Neural Signal Processor and Cereplex M32 headerstage

(Blackrock Microsystems, USA). The signals were analog filtered between 0.3 and 7.5 kHz and subsequently digitally filtered between 0.25 and 5 kHz.

Three different types of mechanical stimulation were applied to the hindpaw corresponding to three different types of functional sensory stimuli (nociception, proprioception and touch). Each stimulus type was applied to varying degrees as we were most interested in differentiating between stimuli that would be carried by the same fiber types.

For nociception the hindpaw was pinched with a pair of forceps that contained a pressure sensor on their tip. The signal from the pressure sensor was used as feedback to apply the same amount of pressure during each pinch, and additionally as a synchronisation signal for the neural recordings. The foot was pinched in two places: the heel and the outer toe (Fig. 2B).

For proprioception the dorsum of the nails were glued to a bar attached to a servo motor. The motor moved the leg to six relative angles,  $\pm 10^\circ$ ,  $20^\circ$  and  $30^\circ$ . A flex sensor attached to the bar was used to provide a synchronisation signal for the neural recordings (Fig. 2C).

For touch, a linear stepper motor was used to touch a Von Frey fiber to the heel of the foot. Two sizes of Von Frey filaments were used 100 g and 300 g. Again a flex sensor attached to the Von Frey filament holder was used to provide a synchronization signal of the filament's movement (Fig. 2D).

Each stimulus was repeated 50 times, for Nociception the stimulus was applied for approximately 1 second with 1 second rest time between stimulus application. By comparison the proprioceptive and touch stimuli were applied for three seconds with three seconds rest between stimulus application.

### D. Data Analysis

The neural recordings were analysed offline to see whether the different stimuli of the same functional type could be discriminated. Three features were extracted to be input into the classification trainer. These were mean absolute value (MAV), root mean square (RMS) and the variance (VAR). All features were calculated during the steady state of stimulus application and not including the transition periods. Features were calculated over the middle 1 second of the nociception stimulus being applied, whereas for proprioception and touch they were calculated over the middle two seconds of stimulus application. For each functional stimulus type the classes were defined as follows:

1) *Nociception*: Three classes consisting of no stimulus, outer toe pinch and heel pinch.

2) *Proprioception*: Seven classes consisting of no stimulus and each of the six angles ( $-30^\circ$ ,  $-20^\circ$ ,  $-10^\circ$ ,  $+10^\circ$ ,  $+20^\circ$  and  $+30^\circ$ ).

3) *Touch*: Three classes consisting of no stimulus, 100 gram touch and 300 gram touch.

Classification was performed using the classification learner application in MATLAB (Mathworks Inc.). Five fold cross validation was used to measure the performance of the

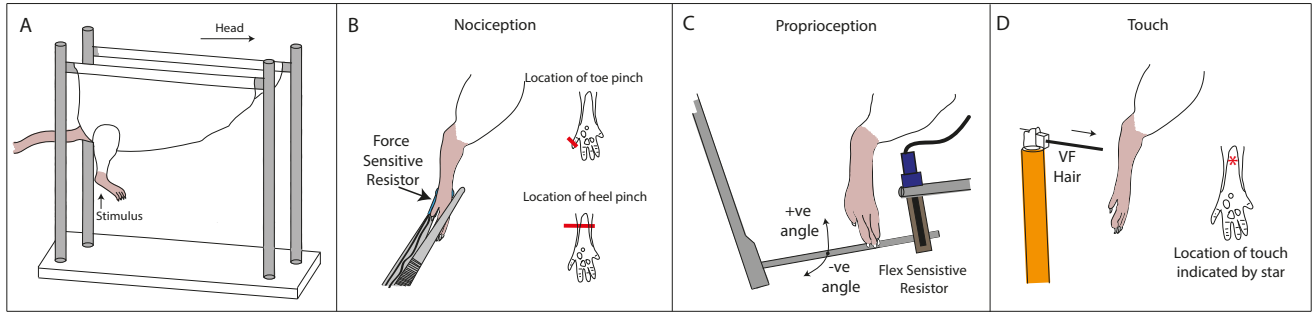


Fig. 2. A) The rat is placed in the sling with his right hindlimb free to be stimulated. All other limbs are kept within the sling. (B) For nociception the paw was pinched into different locations with forceps that contained a force sensitive resistor. (C) For proprioception the dorsum of the nails were glued to a bar attached to a servo motor, the motor rotated the leg to different angles. (D) For touch the heel of the paw was touched with Von Frey fibers.

classifier. The performance of the classifier was determined when using the values calculated on all 16 electrodes and compared to the case where only the information from each of the four rings was available.

### III. RESULTS

The performance of a quadratic support vector machine classifier was examined separately for the three stimulus types applied to the foot. Fig. 3 shows the five fold cross validation error calculated in all three animals for all three features extracted (RMS, MAV and VAR) including the cases where information was available from all 16 electrodes as well as when information was only available from each of the four electrodes on a single ring of the cuff electrode array.

1) *Nociception*: Classification was aimed at discriminating between a pinch of the outer toe, a pinch of the heel or no stimulus being applied. Figure 3A shows that the classifier performed well regardless of the feature used for classification. The highest classification rate of 92.2% occurred in Animal 2, when information from all 16 electrodes and the VAR feature were used. The lowest classification rate with 82.2% of data correctly classified was in Animal 1 when only VAR information was available from ring 2.

2) *Proprioception*: The foot was moved to six different angles (-30, -20, -10, 10, 20 and 30). In Animal 3 the data corresponding to the positive 10 angle was excluded due to noise in the recording. Classification was aimed at discriminating the angle the foot was moved to as well as no stimuli, giving seven different classes (six classes in Animal 3). The highest classification rate was achieved in Animal 2 with 100% of points correctly classified when information from all 16 electrodes with either the RMS or VAR features being extracted. The lowest classification rate (93.4%) occurred in Animal 1 when only VAR information from ring 3 was used.

3) *Touch*: The heel of the foot was touched with Von Frey fibers of two different forces, 100 and 300 grams. Classification was aimed at discriminating between the two different Von Frey fiber forces and no stimulus. The performance of the classifier at discriminating touch stimuli was much lower than seen in the proprioceptive and nociceptive conditions.

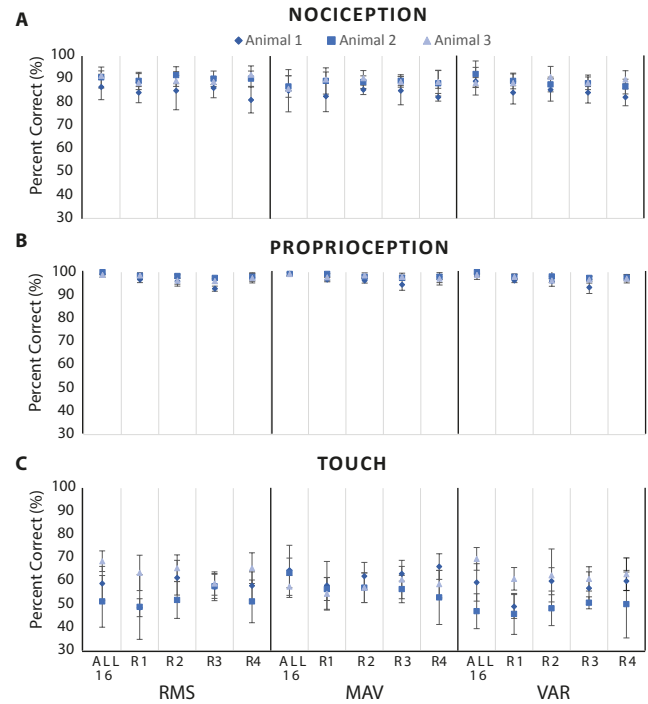


Fig. 3. Performance of quadratic support vector machine in all three animals for the three different stimulus types: A) nociception, B) proprioception and C) touch. The error bars show the standard error and are calculated based on the set of five results calculated in the 5-fold cross validation process. The random chance levels corresponding to the three stimulus types are: 33.3%, 14.4% and 33.3% respectively. The letter "R" stands for ring.

The highest correct classification rate of 69.5% was achieved in Animal 3 and lowest correct classification rate of 42.3% achieved in Animal 2 with RMS. While the classification rates were lower than those seen in the proprioceptive and nociceptive conditions, the performance of the classifier was still above chance (Fig. 3C).

### IV. DISCUSSION

The aim of this study was to develop a better understanding of how a multi-channel cuff could be used to decode afferent sensory signals for use in a closed loop neural prosthesis. In particular we were interested in exploring whether if signals carried along the same fiber type could

be discriminated, as it was shown this was not possible when using a single tripolar cuff in [3]. To this aim we recorded neural signals in response to a range of sensory events corresponding to different types of stimuli. In all cases the classifier performed above chance, regardless of the features used for training.

1) *Nociception*: The classifier was able to discriminate between the three different classes used in Nociception with a high accuracy in all three animals. When information was used from all 16 electrodes the lowest number of correct classifications (85%) occurred in Animal 1 when the MAV feature was used. The classifier was better at discriminating the nociceptive stimuli than the touch. This is in contrast to [3] where they found the nociceptive stimulus to be the most difficult to classify and this was put down to the small size of the fibers that transmit these signals, reducing the signal to noise ratio. It is possible that here we were more easily able to classify the nociceptive than the touch stimulus because of the comparatively large size of the forceps we have used to pinch the foot in our study. This would have resulted in an increase in the number and size of fibers transmitting information about touch and/or proprioception. It is difficult to isolate a pain stimulus that would not evoke other types of sensation to limit this effect. Nevertheless the classifier was able to consistently discriminate between a pinch of the outer toe, a pinch of the heel and no stimulus.

2) *Proprioception*: The classifier was able to discriminate between the seven different classes with a high classification rate in all three animals. Importantly both the direction of the foot movement (extension or flexion) and the size of the movement could be discriminated consistently. This indicates that signals recorded from electrodes placed circumferentially around the nerve can be used to discriminate sensory signals transmitted by the same fiber types. The muscles responsible for flexion and extension are supplied by different branches of the sciatic nerve [11]. It is perhaps not surprising then that these signals could be consistently identified correctly as [7] has previously shown that signals travelling along different branches of the nerve can be classified in multi-channel cuff recordings. Nevertheless, it is likely that signals that are carried along nerve fibers of the same type that are situated close to each other in the nerve will be more difficult to classify.

3) *Touch*: The classification rate of the touch stimuli was above the chance level in all three animals. However, the performance of the classification was the lowest for touch when compared to the other types of stimuli. Using a Von Frey fiber to apply the touch stimulus allows for a stimulus of a reproducible size to be applied to a small area of the foot, eliciting a response in only a small number of fibers. This may be why it is more difficult to classify this signal as fewer fibers were activated reducing the size of the detectable signal. In addition, here we have only examined the steady-state case and not the transient period from no stimulus to touch. Mechanoreceptors can be fast or slow adapting, only

the slow adapting fibers will encode the steady state touch response [12]. Examining the signal during the transition period may be able to shed more light on the size and location of the touch stimulus being applied.

## V. CONCLUSION

The features and classification algorithm used here consistently discriminated sensory stimuli that would be transmitted by the same fiber types with an accuracy of better than chance. The results of this study show that electroneurographic signals recorded from a multi-channel cuff with electrodes placed circumferentially around the nerve provide information both in terms of the type and strength of the stimulus applied. While, classifiers that used information obtained from all 16 electrodes generally outperformed those that used information from four electrodes on a single ring, the difference in performance was small. Future work will examine the performance of the classifier in realtime to estimate the viability of such a classifier in a prosthetic application.

## REFERENCES

- [1] G. S. Dhillon and K. W. Horch, "Direct neural sensory feedback and control of a prosthetic arm," *IEEE Trans. Neu. Sys. Rehab. Eng.*, vol. 13, no. 4, pp. 468–472, 2005.
- [2] X. Navarro, T. B. Krueger, N. Lago, S. Micera, T. Stieglitz, and P. Dario, "A critical review of interfaces with the peripheral nervous system for the control of neuroprostheses and hybrid bionic systems," *J. Peripheral Nervous Sys.*, vol. 10, no. 3, pp. 229–258, 2005.
- [3] S. Raspopovic, J. Carpaneto, E. Udina, X. Navarro, and S. Micera, "On the identification of sensory information from mixed nerves by using single-channel cuff electrodes," *J. NeuroEng. Rehab.*, vol. 7, pp. 1–15, 2011.
- [4] H. A. C. Wark, R. Sharma, K. S. Matthews, E. Fernandez, J. Yoo, B. Christensen, P. Tresco, L. Rieth, F. Solzbacher, and R. A. Normann, "A new high-density (25 electrodes/mm<sup>2</sup>) penetrating microelectrode array for recording and stimulating sub-millimeter neuroanatomical structures," *J. Neural Eng.*, vol. 10, no. 4, p. 045003, 2013.
- [5] J. Badia, S. Raspopovic, J. Carpaneto, and S. Micera, "Spatial and functional selectivity of peripheral nerve signal recording with the transversal intrafascicular multichannel electrode (TIME)," *IEEE Trans. Neur. Sys. Rehab. Eng.*, vol. 24, no. 1, pp. 20–27, 2016.
- [6] L. Citi, J. Carpaneto, K. Yoshida, K.-P. Hoffmann, K. P. Koch, P. Dario, and S. Micera, "On the use of wavelet denoising and spike sorting techniques to process electroneurographic signals recorded using intraneural electrodes," *J. Neurosci. Meth.*, vol. 172, no. 2, pp. 294–302, 2008.
- [7] J. Zariffa, M. K. Nagai, Z. J. Daskalakis, and M. R. Ropovic, "Influence of the number and location of recording contacts on the selectivity of a nerve cuff electrode," *IEEE Trans. Neur. Sys. Rehab. Eng.*, vol. 17, no. 5, pp. 420–427, 2004.
- [8] E. Brunton, C. Blau, and K. Nazarpour, "Multichannel cuff electrodes for peripheral nerve stimulation and recording," in *IEEE Int Conference on Systems, Man, and Cybernetics (SMC)*, 2016, pp. 003 223–003 227.
- [9] P. A. Flecknell and M. Mitchell, "Midazolam and fentanyl-fluanisone: assessment of anaesthetic effects in laboratory rodents and rabbits," *Lab Anim.*, vol. 18, no. 2, pp. 143–146, 1984.
- [10] J. Kortelainen, H. Al-Nashash, A. Vipin, X. Y. Thow, and A. All, "The effect of anaesthesia on somatosensory evoked potential measurement in a rat model," *Laboratory Animals*, vol. 50, pp. 63–66, 2015.
- [11] E. C. Greene, *Anatomy of the rat*. Pub. Amer. Philosoph. Soc. Philadelphia, 1936, vol. 27.
- [12] Å. B. Vallbo and R. S. Johansson, "Properties of cutaneous mechanoreceptors in the human hand related to touch sensation," *Hum Neurobiol.*, vol. 3, no. 1, pp. 3–14, 1984.